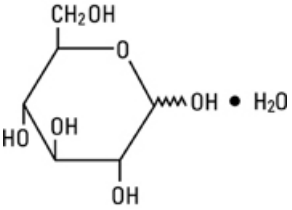
MAGNESIUM SULFATE IN DEXTROSE - magnesium sulfate injection, solution
Hospira, Inc.

Flexible Plastic Container
For Intravenous Use Only
R_x only

DESCRIPTION

Magnesium Sulfate in 5% Dextrose Injection, USP is a sterile, nonpyrogenic solution of magnesium sulfate heptahydrate and dextrose in water for injection. Each 100 mL contains 1 or 2 g magnesium sulfate heptahydrate and dextrose, hydrous 5 g in water for injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment. The pH is 4.5 (3.5 to 6.5). It is available in 1% and 2% concentrations. See HOW SUPPLIED section for the content and characteristics of available dosage forms and sizes.
Magnesium Sulfate, USP heptahydrate is chemically designated $MgSO_4 \cdot 7H_2O$, colorless crystals or white powder freely soluble in water.
Dextrose, USP is chemically designated D-glucose, monohydrate ($C_6H_{12}O_6 \cdot H_2O$), a hexose sugar freely soluble in water. It has the following structural formula:



Molecular weight 198.17.
Water for Injection, USP is chemically designated H_2O.
The flexible plastic container is fabricated from a specially formulated polyvinylchloride. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly. Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials. Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

CLINICAL PHARMACOLOGY

Magnesium (Mg^{++}) is an important cofactor for enzymatic reactions and plays an important role in neurochemical transmission and muscular excitability.
Magnesium prevents or controls convulsions by blocking neuromuscular transmission and decreasing the amount of acetylcholine liberated at the end plate by the motor nerve impulse. Magnesium is said to have a depressant effect on the central nervous system, but it does not adversely affect the mother, fetus or neonate when used as directed in eclampsia or pre-eclampsia. Normal serum magnesium levels range from 1.3 to 2.1 mEq/liter.
As serum magnesium rises above 4 mEq/liter, the deep tendon reflexes are first decreased and then disappear as the serum level approaches 10 mEq/liter. At this level respiratory paralysis may occur. Heart block also may occur at this or lower serum levels of magnesium.
Magnesium acts peripherally to produce vasodilation. With low doses only flushing and sweating occur, but larger doses cause lowering of blood pressure. The central and peripheral effects of magnesium poisoning are antagonized to some extent by intravenous administration of calcium.
With intravenous administration the onset of anticonvulsant action is immediate and lasts about 30 minutes. Following intramuscular administration the onset of action occurs in about one hour and persists for three to four hours. Effective anticonvulsant serum levels range from 2.5 to 7.5 mEq/liter.
Pharmacokinetics:
Absorption: Intravenously administered magnesium is immediately absorbed.
Distribution: Approximately 1-2% of total body magnesium is located in the extracellular fluid space. Magnesium is 30% bound to albumin.
Metabolism: Magnesium is not metabolized.
Excretion: Magnesium is excreted solely by the kidney at a rate proportional to the serum concentration and glomerular filtration.
Special Populations:
Renal Insufficiency: Magnesium is excreted solely by the kidney. In patients with severe renal insufficiency, the dose should be lower and frequent serum magnesium levels must be obtained (see Dosage and Administration).
Hepatic Insufficiency: Magnesium is excreted solely by the kidney. No dosing adjustments are necessary in hepatic insufficiency.
Drug-Drug Interactions: Drug induced renal losses of magnesium occur with the following drugs or drug classes:

Aminoglycosides	Amphotericin B
Cyclosporine	Diuretics
Digitalis	Cisplatin
Alcohol	

INDICATIONS AND USAGE
Magnesium Sulfate in 5% Dextrose Injection, USP is indicated for use as an intravenous anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy. When used judiciously it effectively prevents and controls the convulsions of eclampsia without producing deleterious depression of the central nervous system of the mother or infant. However, other effective drugs are available for this purpose.

CONTRAINDICATIONS
Intravenous magnesium should not be given to mothers with toxemia of pregnancy during the two hours preceding delivery.

WARNINGS
Intravenous use in eclampsia should be reserved for immediate control of life-threatening convulsions.
Parenteral use in the presence of renal insufficiency may lead to magnesium intoxication.

PRECAUTIONS
Because magnesium is removed from the body solely by the kidneys, the drug should be used with caution in patients with renal impairment. Urine output should be maintained at a level of 100 mL every four hours. Monitoring serum magnesium levels and the patient's clinical status is essential to avoid the consequences of overdosage in toxemia. Clinical indications of a safe dosage regimen include the presence of the patellar reflex (knee jerk) and absence of respiratory depression (approximately 16 breaths or more/ minute). Serum magnesium levels usually sufficient to control convulsions range from 3 to 6 mg/100 mL (2.5 to 5 mEq/liter). The strength of the deep tendon reflexes begins to diminish when serum magnesium levels exceed 4 mEq/liter. Reflexes may be absent at 10 mEq magnesium/liter, where respiratory paralysis is a potential hazard. An injectable calcium salt should be immediately available to counteract the potential hazards of magnesium intoxication in eclampsia.
Magnesium Sulfate in 5% Dextrose Injection, USP should be administered slowly to avoid producing hypermagnesemia.

Carcinogenesis, Mutagenesis, Impairment of Fertility:
Studies with Magnesium Sulfate in 5% Dextrose Injection, USP have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

Pregnancy Category A.
Studies in pregnant women have not shown that magnesium sulfate injection increases the risk of fetal abnormalities if administered during all trimesters of pregnancy. If this drug is used during pregnancy, the possibility of fetal harm appears remote. However, because studies cannot rule out the possibility of harm, magnesium sulfate solution should be used during pregnancy only if clearly needed.
When administered by continuous intravenous infusion (especially for more than 24 hours preceding delivery) to control convulsions in toxemic mothers, the newborn may show signs of magnesium toxicity, including neuromuscular or respiratory depression. See OVERDOSAGE.

Nursing Mothers:
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Magnesium Sulfate in 5% Dextrose Injection, USP is administered to a nursing woman.

ADVERSE REACTIONS
The adverse effects of parenterally administered magnesium usually are the result of magnesium intoxication. These include flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac and central nervous system depression proceeding to respiratory paralysis. Hypocalcemia with signs of tetany secondary to magnesium sulfate therapy for eclampsia has been reported.

OVERDOSAGE
Magnesium intoxication is manifested by a sharp drop in blood pressure and respiratory paralysis. Disappearance of the patellar reflex is a useful clinical sign to detect the onset of magnesium intoxication. In the event of overdosage artificial ventilation must be provided until a calcium salt can be injected intravenously to antagonize the effects of magnesium.

In adults intravenous administration of 5 to 10 mEq of 10% calcium gluconate will usually reverse respiratory depression or heart block due to magnesium intoxication. In extreme cases, peritoneal or hemodialysis may be required.
Hypermagnesemia in the newborn may require resuscitation and assisted ventilation via endotracheal intubation or intermittent positive pressure ventilation as well as intravenous calcium.

DOSAGE AND ADMINISTRATION

Magnesium Sulfate in 5% Dextrose Injection, USP is intended for intravenous use only. For the management of pre-eclampsia or eclampsia, intravenous infusions of dilute solutions of magnesium (1% to 8%) are often given in combination with intramuscular injections of 50% Magnesium Sulfate Injection, USP. Therefore, in the clinical conditions cited below, both forms of therapy are noted, as appropriate.

In Eclampsia

In severe pre-eclampsia or eclampsia, the total initial dose is 10 to 14 g of magnesium sulfate. To initiate therapy, 4 g of Magnesium Sulfate in 5% Dextrose Injection, USP may be administered intravenously. The rate of I.V. infusion should generally not exceed 150 mg/minute, or 7.5 mL of a 2% concentration (or its equivalent) per minute, except in severe eclampsia with seizures. Simultaneously, 4 to 5 g (32.5 to 40.6 mEq) of magnesium sulfate may be administered intramuscularly into each buttock using undiluted 50% Magnesium Sulfate Injection, USP. After the initial I.V. dose, some clinicians administer 1-2 g/hour by constant I.V. infusion. Subsequent intramuscular doses of 4 to 5 g of magnesium sulfate may be injected into alternate buttocks every four hours, depending on the continuing presence of the patellar reflex, adequate respiratory function, and absence of signs of magnesium toxicity. Therapy should continue until paroxysms cease.
A serum magnesium level of 6 mg/100 mL is considered optimal for control of seizures. A total daily (24 hr) dose of 30 to 40 g magnesium sulfate should not be exceeded. In the presence of severe renal insufficiency, frequent serum magnesium concentrations must be obtained, and the maximum recommended dosage of magnesium sulfate is 20 g per 48 hours.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
Do not administer unless solution is clear. Discard unused portion.

HOW SUPPLIED

Magnesium Sulfate in 5% Dextrose Injection, USP is supplied in single-dose flexible plastic containers as follows:

NDC	Size Container	Total Magnesium Sulfate*	Total Magnesium Ion	Magnesium Sulfate* Concentration	Magnesium Ion Concentration	Osmolarity (calc.)
0409-6727-23	100 mL	1 g	8.1 mEq	1% (10 mg/mL)	8.1 mEq/100 mL	333 mOsmol/Liter
0409-6728-03	500 mL	10 g	81.1 mEq	2% (20 mg/mL)	16.2 mEq/100 mL	415 mOsmol/Liter
0409-6728-09	1000 mL	20 g	162.3 mEq	2% (20 mg/mL)	16.2 mEq/100 mL	415 mOsmol/Liter

*As the heptahydrate.

WARNING: DO NOT USE FLEXIBLE CONTAINER IN SERIES CONNECTIONS.

Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.] Protect from freezing.
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